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ORIGINAL ARTICLE

Body mass index, physical activity, and risk of renal cell carcinoma

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Objective: To investigate the association between obesity and risk of renal cell carcinoma and to examine whether the association is modified by physical activity.
Subjects: A population-based case–control study of 406 patients with renal cell carcinoma and 2434 controls conducted in Iowa.
Methods: Information was collected on weight at the ages 20–29, 40–49, and 60–69 years, height, nonoccupational physical activity, diet, and other lifestyle factors. Renal cell carcinoma risk was estimated by odds ratios (ORs) and 95% confidence intervals (CIs), adjusting for age, total energy intake, and other confounding factors.
Results: Height and total energy intake were not associated with risk in either sex. In men, neither physical activity nor level of obesity in any period of life was significantly associated with risk. In women, lower physical activity was associated with higher risk (OR = 2.5; 95% CI = 1.2–5.2 comparing exercise <1 time/month to >1 time/day). Compared with women in the lowest quartile for BMI, the risks of renal cell carcinoma for women in the highest 10% of BMI in their 20s, 40s, and 60s were 1.4 (CI = 0.6–3.1), 1.9 (CI = 0.9–4.2), and 2.3 (CI = 0.9–6.0), respectively. When analyses were limited to self-respondent data, the corresponding ORs were 2.9 (CI = 1.2–7.4), 3.2 (CI = 1.3–7.5), and 2.1 (CI = 0.7–6.4), respectively. There was little evidence that physical activity modifies the association of BMI with renal cell carcinoma.
Conclusion: Nonoccupational physical activity was inversely associated and obesity was positively associated with risk of renal cell carcinoma among women. The risk appeared to be greater for women in the highest 10% of BMI in their 40s. Our finding of little evidence of an interaction between physical activity and BMI requires confirmation.
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Keywords: body mass index; physical activity; renal cell carcinoma

Introduction

The incidence of renal cell carcinoma, the predominant type of kidney cancer, has increased at a rate of 2–4% per year since the 1970s in the US.[1] Although renal cell carcinoma accounts for only 3% of adult malignancies, its incidence has increased compared with other cancers. This increase cannot be fully explained by early detection of presymptomatic tumors.[2]

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Overweight and obesity (expressed as body mass index (BMI)) have been consistently associated with an elevated risk of renal cell carcinoma among women,[3–9] and to a lesser degree, among men.[4,8,10–12] Physical activity was inversely associated with risk of renal cell carcinoma in some,[4,13–15] but not all[8,12,16,17] studies. There is variation among studies regarding the degree and time period of adulthood overweight that is associated with risk.[5–7,12] In addition, although body weight is modulated by metabolic factors, diet, and physical activity, few studies[8,9,11,13,18] have tried to disentangle the effects of obesity from diet and physical activity. To further evaluate the association of obesity, as expressed by BMI, with the risk of renal cell carcinoma, and to explore the inter-relationship between BMI and physical activity, we analyzed renal cell carcinoma data collected as part of a population-based case–control study of six cancer sites (bladder, kidney, pancreas, colon, rectum, and brain).

Material and methods

Study population

A population-based, multicancer case–control study was conducted in Iowa between 1986 and 1990. The study was approved by an institutional review board at the University of Iowa. Detailed methods have been reported elsewhere.[19] Briefly, eligible cases were residents of the state of Iowa, aged 40–85 years, newly diagnosed with histologically confirmed renal cell carcinoma (ICD-O code 189.0). Cases were identified by the State Health Registry of Iowa, the state's cancer registry.[1] Of the 463 eligible cases, 406 participated (87.7% response rate). Of the 406 renal cell carcinoma cases sent self-respondent questionnaires, 206 questionnaires were completed by the subject, 119 were completed by another person (proxy), and 81 cases were not asked who had completed the form. It is likely that most of these 81 subjects were self-respondents because (1) they requested a questionnaire whose wording was designed for self-respondents (prior to inclusion of the relevant question about proxy completion), and (2) among those who were sent a later version of this questionnaire with the proxy question, only 11% indicated that it was completed by someone other than the subject.

Controls were frequency-matched to cases of all six cancer types combined by gender and 5-year age groups, resulting in a matching ratio ranging from 1.7:1 for bladder cancer to approximately 6.5:1 for pancreatic cancer. Controls under 65 years of age were selected randomly from the computerized State of Iowa driver's license records, whereas controls aged 65 years and more were selected randomly from lists provided by the US Health Care Financing Administration, now known as the Centers for Medicare and Medicaid Services. Both of these sampling frames have been shown to achieve greater than 95% coverage of the intended population.[20,21] Of the 999 eligible controls under the age of 65 years, 817 participated (82% response rate), whereas 1617 of 2036 eligible controls aged 65 years or more participated (79% response rate). Of the 2434 controls, 2064 were self-respondents, 243 were proxies, and 127 were not determined. As for the cases, most of these 127 questionnaires were possibly completed by the study subject.

Data collection

Data were collected with a mailed questionnaire supplemented by a telephone interview. The questionnaire included information on demographics, anthropometric measures (weight history in their 20s, 40s, and 60s, as well as usual adult height), usual nonoccupational physical activity, smoking history, a 55-item food frequency questionnaire, occupational history, past medical history (including self-report of physician-diagnosed hypertension and history of bladder/kidney infection), history of cancer among first degree relatives, and lifetime residential history. Information on usual nonoccupational physical activity was obtained from the following question: 'During most of your adult life, how often did you usually do strenuous or moderate physical exercise such as jogging, swimming laps, gardening, or walking briskly for 10 min? Please do not include physical activities connected with any jobs you may have held.'

Subjects who expressed reluctance to complete the detailed questionnaire at the initial telephone contact or at any time afterwards were offered an alternative 15-min telephone interview that included questions essential to the present report. Of 406 cases, 374 (92%) completed the mailed questionnaire, five (1%) completed a full-length telephone interview, and 27 (7%) completed the abbreviated telephone interview. Corresponding numbers for controls were 2164 (89%), 102 (4%), and 168 (7%), respectively.

Data analysis

BMI, an indirect measure of adiposity, was calculated as weight divided by the square of height (kg/m^2), using the self-report of usual adult height and weight during three different periods of a subject's life (20s, 40s, and 60s). The variables were grouped into quartiles, separately for men and women, based on the distribution among controls, with the last quartile further divided into the 76–90 percentile and 91–100 percentile (upper decile) (Table A1 in Appendix A). Anthropometric factors were developed for each period of life. To evaluate possible effect modification of the obesity-renal cell carcinoma association by nonoccupational physical activity, the analyses were conducted separately for individuals who were physically inactive (strenuous or moderate activity 1–4 times/month, <1 time/month, or never) or physically active (2–6 times/week or >1 time/day). Total energy intake was calculated using the consumption frequency data from the questionnaire, and sex-specific portion sizes and food consumption data from the NHANES II nutrient database.[22]

Three measurements were developed to investigate the effect of weight changes: the absolute change in BMI per period of life, the variability in BMI, and the relative change in BMI. The variability in BMI was computed as the coefficient of variation around the regression line determined from a multivariate logistic model, thus eliminating the portion of the variability that can be attributed to the progressive systematic change in BMI. The relative change in BMI was calculated as the difference between BMI at a later period of life and BMI at an earlier period, divided by BMI at the earlier period.

To evaluate the effect of proxy respondents on the risk estimate, we obtained from the 1985 Iowa driver's license database information on height and weight, which was provided at the time of license renewal. The year 1985 was chosen because height and weight preceded the date of diagnosis of renal cell carcinoma in most of the cases. The intraclass correlations for weight during ages 20–29, 40–49, and 60–69 years reported by proxies in the questionnaire and by subjects themselves in the driver's license file were 0.32,

0.69, and 0.81, respectively, for men, and were 0.10, 0.52, and 0.77, respectively, for women. Corresponding correlations for self-respondent data in the questionnaire compared to driver's license data were 0.35, 0.73, 0.99, respectively, for men, and 0.31, 0.76, and 0.85, respectively, for women. The strong correlations suggest that proxies may be able to provide reliable information on weight (except weight in their 20s) for estimating risk. Therefore, proxy data for 200 cases and 370 controls were included to increase the statistical power in the analysis of the potential interaction between BMI and nonoccupational physical activity.

The maximum likelihood estimate of the odds ratio (OR) with 95% confidence interval (CI)[23] was used as the measure of association between anthropometric variables and risk of renal cell carcinoma. Multiple logistic regression analysis was used to adjust for potential confounding variables in this data set, including age (continuous), history of high blood pressure (yes, no), education (continuous), marital status (females only; married, not married), smoking (never, former, and current), family history of kidney cancer (yes, no), nonoccupational physical activity (where warranted), total energy intake (continuous), and consumption of red meat (continuous) and vegetables (continuous). Multivariate modeling was performed separately for men and women. Tests for trend across the quartiles were performed through logistic regression by classifying the first to fourth quartiles as an ordinal variable. We also tested for trend by modeling anthropometric variables as continuous variables. No meaningful differences were noted between the two methods. Therefore, we present in the table the *P*-trend values derived from ordinal variables. To test for statistical interaction between nonoccupational physical activity and BMI, we first fit the main effect model with physical activity as a single dummy variable (physically active and physically inactive) and BMI as three dummy variables. Crossproduct terms were then calculated and included with the main effects. The -2 log likelihood estimates for the main effects were then compared to that for the model including the interaction terms.

Results

Characteristics of study subjects and possible risk factors for renal cell carcinoma are shown in Table 1. Compared with controls, cases were younger, consumed more red meat and fewer vegetables, and weighed more during all three periods of life. Cases were also more likely to be current smokers, currently married (females only), and more likely to report a history of hypertension and a family history of kidney cancer among first-degree relatives.

Lower physical activity was associated with a higher risk of renal cell carcinoma in women (Table 2). Compared with women who exercised daily, the ORs were 2.5 (95% CI = 1.2–5.2) for those who exercised less than once a month or never. The point estimates were not attenuated after additional adjustment for BMI (data not shown). However, the pattern of increased risk was not monotonic with our measure of self-reported activity.

There is little evidence that BMI was associated with the risk of renal cell carcinoma among men, irrespective of exclusion or inclusion of proxy data (Table 2). When BMI was evaluated in continuous form, there was a weak association between BMI at ages in the 20s and 40s, but not in the 60s, with the risk of renal cell carcinoma (data not shown). In women, BMI was associated with the risk of renal cell carcinoma, and the risk appeared to be stronger among those in the highest 10% of BMI where the ORs for BMI in their 20s, 40s, and 60s were 1.4 (95% CI = 0.6–3.1), 1.9 (95% CI = 0.9–4.2), and 2.3 (95% CI = 0.9–6.0), respectively, compared with women in the lowest quartile for BMI. When analyses were limited to self-respondent data, the corresponding ORs were 2.9 (95% CI = 1.2–7.4), 3.2 (CI = 1.3–7.5), and 2.1 (CI = 0.7–6.4), respectively. When BMI was evaluated in continuous form, each higher unit of BMI was associated with a 7–10% higher risk of renal cell carcinoma, depending on the decade of age for which weight was estimated (data not shown). None of our three measurements of changes in BMI across three different periods of life were associated with risk of renal cell carcinoma in either men or women (data not shown).

Table 3 shows the joint effects of physical activity and BMI where the reference group was subjects who were physically active (i.e., exercise 2–6/week or >1/day) and in the lowest quartile of BMI. There was little evidence of an interaction between physical activity and BMI in either men or women.

Discussion

Results from this population-based case–control study support previous observations linking a higher BMI to an excess risk of renal cell carcinoma in women, and provide little evidence for an association in men. The elevated risks tend to exist for those individuals in the higher or highest reported groups of BMI. Nonoccupational physical activity was inversely associated with the risk of renal cell carcinoma in women. There was little evidence that physical activity modified the association between BMI and renal cell carcinoma.

The rapid increase in the incidence of renal cell carcinoma in the US has paralleled a rising prevalence of obesity (increased 31% from 1976 to 1991 and 61% between 1991 and 2000),[24], and, thus, obesity might explain, at least partly, the upward trend in incidence. Previous investigations of the relationship of BMI with renal cell carcinoma risk consistently found an association among women,[3–9,12] and our results support these findings. Our finding of the greatest risk with high level of BMI (i.e., top 10% of BMI) among women is also in agreement with previous studies,[4,8,11,12,18,25] even though the cutpoints for the top 10% of BMI in the present study are, in general, smaller than those found in previous

Table 1 Relation of potential confounding factors to case–control status by sex, Iowa, 1986–1990

Factor	*Males*					*Females*				P-*value*
	Cases (n = *261*)		*Controls* (n = *1601*)			*Cases* (n = *145*)		*Controls* (n = *833*)		
	Mean (s.d.)	*%*	*Mean (s.d.)*	*%*	P-*value*	*Mean (s.d.)*	*%*	*Mean (s.d.)*	*%*	
Age (years)	64 (9.5)		68 (9.7)			65 (9.6)		68 (10.4)		
Total energy intake (Kcal/d)	2100 (1036.6)		1984 (809.7)		0.3	1364 (456.8)		1368 (509.5)		0.9
Red meat (servings/d)	1.7 (0.99)		1.5 (1.05)		0.6	1.5 (1.03)		1.3 (1.78)		0.1
Vegetables (servings/d)	1.5 (1.17)		1.6 (1.27)		0.005	1.4 (0.85)		1.9 (1.40)		<0.001
Height (m)	1.8 (0.07)		1.8 (0.06)		0.2	1.6 (0.07)		1.6 (0.06)		0.2
Weight in the 20s	74.4 (12.35)		70.8 (10.73)		0.002	59.3 (9.97)		56.3 (8.32)		0.004
Weight in the 40s	81.4 (14.25)		77.64 (12.17)		0.02	69.3 (15.62)		62.8 (9.94)		<0.001
Weight in the 60s	81.5 (14.22)		80.6 (12.28)		0.9	70.7 (14.86)		65.7 (10.92)		0.001
Current marital status										
Married		87		86			67		56	
Not married		13		14	0.4		32		44	0.3
Missing		0		0			1		0	
Education										
<High school		20		24			18		14	
High school		52		49			58		54	
>High school		26		25	0.7		23		31	0.01
Missing		2		2			1		1	
Smoking status										
Never		23		33			63		69	
Former		44		46			12		14	
Current		34		20	<0.001		24		17	0.3
Missing		9		1			1		0	
History of hypertension										
No		49		62			45		52	
Yes		40		31	<0.001		51		38	0.002
Missing		11		7			4		10	
Family history of kidney cancer										
No		97		99			95		98	
Yes		3		1	0.1		5		2	0.01

studies. Among men, the literature is less consistent. Although some studies suggest that the strength of the association for men is as large as that for women,[9–11] others have found no association with BMI for men.[4,8,12]

It is not clear why the association with obesity is stronger among women than men. It is possible that the accuracy of self-reported height and weight differ by gender. Alternatively, the gender difference in risk suggests a possible role of the pattern of body fat distribution. Women tend to store fat in the gluteal-femoral region, whereas men store fat in the visceral (abdominal) depot.[26] The degree of obesity and the distribution of fat tissue have been linked to distinct patterns of hormonal changes (e.g., insulin-like growth factor I),[27] but the implications for renal carcinogenesis are not well understood. Another possible explanation is that sex-specific risk factors, such as a hormonal factor, may be important in renal carcinogenesis. Obesity increases the levels of free endogenous estrogens,[28] which might affect renal cell proliferation and growth, and thereby carcinogenesis.

Findings from studies that evaluated the magnitude and time period of adulthood overweight in relation to the risk of renal cell carcinoma are inconsistent. Two population-based case–control studies found positive associations at all ages except at the age of 20 years.[5,6] In contrast, a hospital-based case–control study showed that the risk was greatest for a high BMI at the age of 20 years for men and women, and the risk continued into adulthood.[7] A population-based case–control study found that higher risk was most evident for

Table 2 Odds ratio (OR) and 95% confidence intervals (CI) for renal cell carcinoma in men and women according to nonoccupational physical activity and body mass index, Iowa, 1986–1990

	Males				*Females*			
	No. of cases[a]	*No. of controls*[a]	*OR (95% CI)*[b]	*OR (95% CI)*[c]	*No. of cases*[a]	*No. of controls*[a]	*OR (95% CI)*[b]	*OR (95% CI)*[c]
Nonoccupational physical activity								
>1/day	32	279	1.0 (referent)	1.0 (referent)	19	155	1.0 (referent)	1.0 (referent)
2–6/week	56	398	1.2 (0.6–2.5)	1.2 (0.7–2.3)	44	247	2.1 (0.8–5.1)	2.2 (1.0–4.5)
1–4/month	42	208	1.2 (0.5–2.7)	1.1 (0.7–2.3)	26	129	1.1 (0.4–3.2)	1.9 (0.9–4.3)
<1/month	95	550	1.5 (0.7–3.2)	1.2 (0.7–2.1)	44	175	2.2 (0.8–5.5)	2.5 (1.2–5.2)
P-trend			*P = 0.6*	*P = 0.9*			*P = 0.2*	*P = 0.1*
BMI in the 20s								
Q1	43	376	1.0 (referent)	1.0 (referent)	32	177	1.0 (referent)	1.0 (referent)
Q2	49	364	0.8 (0.4–1.6)	1.4 (0.8–2.4)	25	177	1.2 (0.5–3.1)	0.7 (0.3–1.4)
Q3	55	336	0.9 (0.5–1.8)	1.4 (0.8–2.5)	29	175	1.1 (0.4–2.9)	0.8 (0.4–1.6)
76–90% Q4	35	222	0.8 (0.4–1.7)	1.2 (0.6–2.2)	23	108	2.4 (0.9–6.4)	1.6 (0.7–3.3)
91–100% Q4	41	147	1.3 (0.6–2.8)	1.8 (1.0–3.3)	22	67	2.9 (1.2–7.4)	1.4 (0.6–3.1)
P-trend			*P = 0.6*	*P = 0.4*			*P = 0.1*	*P = 0.1*
BMI in the 40s								
Q1	38	363	1.0 (referent)	1.0 (referent)	23	170	1.0 (referent)	1.0 (referent)
Q2	48	361	1.0 (0.5–2.3)	1.3 (0.7–2.3)	20	194	0.5 (0.2–1.4)	0.5 (0.2–1.1)
Q3	66	345	1.5 (0.8–3.1)	2.0 (1.1–3.5)	33	162	1.1 (0.4–2.7)	1.3 (0.6–2.7)
76–90% Q4	41	236	1.5 (0.7–3.3)	1.5 (0.8–2.8)	29	110	1.1 (0.4–2.9)	1.7 (0.8–3.6)
91–100% Q4	37	144	1.1 (0.4–2.6)	1.7 (0.9–3.3)	26	67	3.2 (1.3–7.5)	1.9 (0.9–4.2)
P-trend			*P = 0.6*	*P = 0.2*			*P = 0.01*	*P = 0.01*
BMI in the 60s								
Q1	49	298	1.0 (referent)	1.0 (referent)	23	142	1.0 (referent)	1.0 (referent)
Q2	33	314	0.5 (0.2–1.4)	0.6 (0.3–1.1)	18	145	0.5 (0.1–1.7)	0.5 (0.2–1.4)
Q3	34	285	0.8 (0.3–1.8)	0.6 (0.3–1.1)	20	146	1.1 (0.4–3.2)	1.0 (0.4–2.5)
76–90% Q4	27	183	1.5 (0.6–3.5)	0.8 (0.4–1.7)	13	86	0.7 (0.2–2.5)	0.7 (0.3–2.1)
91–100% Q4	20	118	0.4 (0.1–1.3)	0.4 (0.2–1.0)	21	54	2.1 (0.7–6.4)	2.3 (0.9–6.0)
P-trend			*P = 0.9*	*P = 0.2*			*P = 0.2*	*P = 0.1*

[a]The total number of cases and controls may not addup to the total in Table 1 because to missing information or nonapplicability (for example, a subject is younger than 60 years of age and does not provide a weight for age in the 60s). [b]Self-respondents only. OR adjusted for age, total energy intake, intake of red meat, intake of vegetables, high blood pressure, education, smoking, family history of kidney cancer, and marital status (females only). [c]All respondents. OR adjusted for age, total energy intake, intake of red meat, intake of vegetables, high blood pressure, education, smoking, family history of kidney cancer, proxy, and marital status (females only).

high BMI in ages 30–50 years in women, but not in men.[12] In the present study, an excess risk was found among individuals who had a high BMI during their 40s, and to a lesser extent, during their 20s, but the difference was not significant. The timing of weight gain during periods of hormonal changes may have different biological effects, especially secondary to differences in the localization of body fat during these periods.[29,30] For example, women with a high BMI in late adolescence or early adulthood have a greater exposure to endogenous androgens and estrogens.[31] Weight gain in adulthood has been found to be more significantly related to the risk of breast cancer[32] and endometrial cancer[33] than weight itself. However, it is still not clear if the timing of weight gain is also important in renal carcinogenesis.

In the present study, low nonoccupational physical activity was associated with an elevated risk of renal cell carcinoma among women. Results from studies[4,8,12–17] that have assessed physical activity in relation to the risk of renal cell carcinoma are inconsistent. Two studies[4,15] showed an inverse association with occupational physical activity, two[13,14] found an inverse association with leisure-time physical activity but not occupational physical activity, whereas the others[8,12,16,17] reported no association with either occupational or leisure-time physical activity. The reason for the observed gender difference in the current study is not clear, but these findings should be viewed cautiously. Our data were limited to nonoccupational physical activity with no information on activity at work, which may be more important for males. Although recreational physical activity is becoming a greater component of overall activity for most adults in the US,[34] our measurement is admittedly crude and lacks information on intensity, frequency, and duration of activity at multiple time-periods during life. These limitations may also explain our findings of no interaction between physical activity and BMI in either men or women. However, two studies[8,13] also found no association of physical activity at work or leisure time with the risk of renal cell carcinoma regardless of the level of BMI.

Table 3 Odds ratio (OR)[a] and 95% confidence intervals (CI) for renal cell carcinoma in men and women according to level of body mass index by nonoccupational physical activity, Iowa, 1986–1990

Anthropometric characteristics	*Males*				*Females*			
	Physically active		*Physically inactive*		*Physically active*		*Physically inactive*	
	OR	*95% CI*	*OR*	*95% CI*	*OR*	*95% CI*	*OR*	*95% CI*
BMI in the 20s								
Q1	**1.0**	—	1.4	0.6–3.2	1.0	—	1.7	0.6–4.5
Q2	1.2	0.5–2.9	2.0	0.9–4.6	0.8	0.3–2.3	0.9	0.3–2.9
Q3	2.1	0.9–5.0	1.4	0.6–3.4	0.8	0.3–2.4	1.3	0.5–3.3
Q4	1.6	0.7–3.7	1.8	0.8–4.0	1.8	0.7–4.6	2.2	0.8–5.7
P-interaction				*P = 0.3*				*P = 0.9*
BMI in the 40s								
Q1	**1.0**	—	1.2	0.5–3.0	1.0	—	0.9	0.3–2.8
Q2	1.2	0.5–3.1	1.5	0.7–3.6	0.3	0.1–1.0	0.7	0.2–2.0
Q3	2.0	0.8–4.6	2.3	1.0–5.2	0.7	0.3–2.0	2.1	0.8–5.6
Q4	1.7	0.7–4.1	1.7	0.7–3.9	2.2	0.9–5.4	1.5	0.6–3.6
P-interaction				*P = 0.9*				*P = 0.1*
BMI in the 60s								
Q1	**1.0**	—	0.8	0.4–2.0	1.0	—	0.9	0.3–3.0
Q2	0.5	0.2–1.2	0.5	0.2–1.4	0.5	0.1–1.9	0.6	0.2–2.4
Q3	0.3	0.1–0.9	0.7	0.3–1.7	0.7	0.2–2.6	1.6	0.5–5.0
Q4	0.8	0.3–1.9	0.5	0.2–1.2	0.9	0.3–2.9	2.0	0.7–5.8
P-interaction				*P = 0.3*				*P = 0.7*

[a]All respondents. OR adjusted for age, total energy intake, intake of red meat, intake of vegetables, high blood pressure, education, smoking, family history of kidney cancer, proxy and marital status (females only).

A major strength of the present study was our ability to make extensive adjustment for potential confounders, including diet, nonoccupational physical activity, smoking, and medical history. Control for total energy intake and physical activity may be particularly important because energy expenditure is an important determinant of adult weight and obesity. However, only a few studies[8,11,18] have tried to disentangle the effects of obesity from diet and physical activity. Other strengths of this study included high response rates (88% for cases and 80% for controls), inclusion of only newly diagnosed, histologically confirmed cases of renal cell carcinoma that occurred in defined time periods in a single geographic area, and randomly selected control subjects representative of the population at large in the targeted geographic area.

One limitation of the present study is that our data on height and weight were self-reported. Although self-reported height and weight are highly correlated with measured height and weight,[35,36] and weight at a young adult age is recalled 20–30 years later with high validity,[37] obese individuals tend to underreport their weight, whereas underweight subjects in general overestimate their body size.[35,38] This might lead to nondifferential misclassification, which could underestimate the true association between obesity and renal cell carcinoma, and, therefore, cannot explain our finding of a positive association among women. Another potential limitation is that only one estimate of nonoccupational physical activity was available for the three different periods in life for which data on BMI were collected. This limited our ability to adequately disentangle the effects of obesity from physical activity. Furthermore, we had no direct measure of adiposity or of lean body mass and no measure of central adiposity, such as the waist-to-hip ratio. Finally, some associations may be observed by chance owing to multiple comparisons, although the associations observed are, in general, consistent with previous studies.

In summary, nonoccupational physical activity was inversely associated with the risk of renal cell carcinoma among women. Our data support obesity as a risk factor for renal cell carcinoma in women, independent of physical activity and total energy intake. The elevated risks tend to exist for those individuals in the higher or highest reported groups of BMI. In addition, the risk for developing renal cell carcinoma appeared to be greater for women in the highest 10% of BMI in their 40s. Our finding of no effect modification of the BMI-renal cell carcinoma association by physical activity requires confirmation. Future studies should critically evaluate the effect of the overall degree of adiposity and the location of fat deposits as well as the frequency, duration, and intensity of occupational and recreational physical activity at various periods of life on the risk of renal cell carcinoma.

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Appendix A

Table A1 Cutpoints for quartiles (Q1, Q2, Q3, Q4) of height, weight, and body mass index by sex

Anthropometric factors	*Quartile*				
	Q1 (Low)	*Q2*	*Q3*	*76–90% Q4*	*91–100% Q4*
Height, m					
Males	⩽1.72	1.73–1.77	1.78–1.82	1.83–1.87	⩾1.88
Females	⩽1.56	1.57–1.62	1.63–1.67	1.68–1.72	⩾1.73
BMI in the 20s (kg/m^2)					
Males	⩽20.44	20.45–22.19	22.20–24.08	24.09–25.85	⩾25.86
Females	⩽19.26	19.27–20.60	20.61–22.49	22.50–24.55	⩾24.56
BMI in the 40s (kg/m^2)					
Males	⩽22.20	22.21–24.25	24.26–26.47	26.48–28.89	⩾28.90
Females	⩽21.17	21.18–23.01	23.02–25.59	25.60–28.26	⩾28.27
BMI in the 60s (kg/m^2)					
Males	⩽23.48	23.49–25.17	25.18–27.35	27.36–30.07	⩾30.08
Females	⩽22.20	22.21–24.32	24.33–27.31	27.33–30.13	⩾30.14